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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/932,812	08/17/2001	Lee-Hwei K. Sun	02SUN2001	5834
7590 06/03/2004				
Hsiang-ning Sun 4212 Villanova Houston, TX 77005				
EXAMINER DEBERRY, REGINA M				
ART UNIT		PAPER NUMBER		
1647				

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/932,812	<b>Applicant(s)</b> SUN ET AL.	
	<b>Examiner</b> Regina M. DeBerry	<b>Art Unit</b> 1647	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 4,5 and 16-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,6-15 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Status of Application, Amendments and/or Claims***

The amendment filed 22 March 2004 has been entered in full. Claims 1-3, 6-15 and 20 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Withdrawn Objections And/Or Rejections***

The rejection of claims 1, 2, 6-8, 10 and 11 under 35 U.S.C. 102(b) as being anticipated by Sudo *et al.*, (WO 99/58662, 11/18/99, in English EP 1 088 888 A1) as set forth at pages 2-3 of the previous Office Action (09 March 2004) is *withdrawn* in view of Applicant's arguments and the instant specification which teaches the cloning of the EPO fragment to the 5' end of the peptide linker.

The rejection of claims 1, 2, 10, 12 and 13 under 35 U.S.C. 103(a) as being unpatentable over Sudo *et al.*, (WO 99/58662, 11/18/99) in view of Sytkowski *et al.* (Journal of Biological Chemistry 274:24773-24778, 1999) as set forth at pages 3-4 of the previous Office Action (09 March 2004) is *withdrawn* in view of Applicant's arguments and the instant specification which teaches the cloning of the EPO fragment to the 5' end of the peptide linker.

The rejection of claims 7-10 and 20 under 35 U.S.C. 112, second paragraph, as set forth at pages 4-5 of the previous Office Action (09 March 2004) is *withdrawn* in view of the amendment (22 March 2004).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 9, 14, 15 and 20 rejected under 35 U.S.C. 112, first paragraph,  
because the specification, while being enabling for:

a human IgG Fc variant **consisting** of a hinge, CH2, and CH3 domains of  
human IgG2 with Pro331Ser mutation as SEQ ID NO:18,

does not reasonably provide enablement for:

a human IgG Fc variant **comprising** a hinge, CH2, and CH3 domains of human  
IgG2 with Pro331Ser mutation as SEQ ID NO:18.

The specification does not enable any person skilled in the art to which it  
pertains, or with which it is most nearly connected, to make and/or use the invention  
commensurate in scope with these claims.

The instant specification teaches the cloning of HuEPO-L-vFc fusion proteins.  
The instant fusion protein contains an IgG Fc variant, which consist of a hinge, a CH2  
and a CH3 domain wherein a specific amino acid mutation is made within the CH2  
domain. The instant claims recite open language, which allows for the IgG Fc variant to  
comprise other sequences and allow for other mutations, variants, etc. The instant  
working examples, however teach a biological function with *specific IgG Fc variants*.  
While it is known that many amino acid substitutions are generally possible in any given

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protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517). Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the structure and still maintain sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

### **Claim Rejections - 35 USC § 102(a)**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 6-8, 10-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Cox *et al.*, WO 01/03737.

Cox *et al.* teach method of making fusion proteins comprising a growth factor fused to a peptide linker fused to an immunoglobulin domain (abstract). Peptide linkers include a mixture of glycine and serine residues (page 5, line 39-page 6, line 2; page 7, lines 27-34; page 9, lines 5-10 and page 22, lines 11-21). Examples of growth factors include erythropoietin (page 6, lines 5-7, page 7, lines 5-26). Cox *et al.* teach variants in the Fc region (page 7, lines 35-38). Cox *et al.* teach EPO-L-vFc (page 8, lines 13-18). Cox *et al.* teach the use of CHO cells to produce the fusion protein (page 9, lines 32-34). Cox *et al.* teach the growth factor/Fc fusion protein containing two or four amino acid linkers (page 22, lines 11-21; page 24, line 26-page 26, line 28).

Cox *et al.* do not explicitly state that the EPO fusion protein exhibits an enhanced in vitro biological activity of at least 2 fold relative to that of recombinant EPO on a molar basis, or the amount of fusion protein produced in a CHO cell line transfected with said fusion protein. However, the prior art structure has all the features required to perform

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the activity recited in the claims. Furthermore, as there are no claimed distinguishing features between the fusion protein of Cox *et al.*, the biological activity would be an inherent feature of the product. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963))

***Conclusion***


No claims are allowed.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
RMD  
5/24/04

  
ELIZABETH KEMMERER  
PRIMARY EXAMINER